1088-120 Left Ventricle Systolic Dysfunction, Total Mortality, and Sudden Death in Patients With Myocardial Infarction Treated With N-3 Polyunsaturated Fatty Acids

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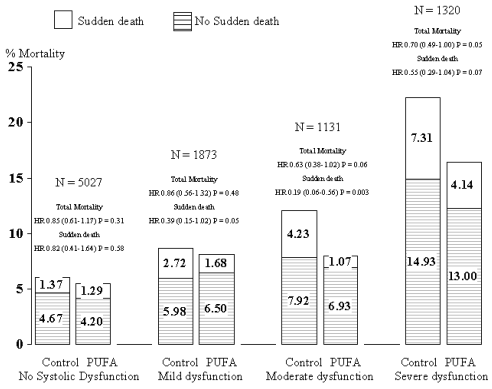
Background: Severe left ventricular systolic dysfunction (LVSD) after myocardial infarction (MI) increases the risk of heart failure, mortality (M) and sudden death (SD). Several treatments reduce M and SD in this cohort. Less information is available on the association between mild/moderate LVSD, M and particularly SD. N-3 polyunsaturated fatty acids (n-3) reduced M and SD in post-MI, but the effect in patient with LVSD is unknown.
Methods: We selected 9351 post-MI patients from the GISSI-Prevenzione trial who had a measurement of ejection fraction (EF). LVSD was classified as absent, EF > 50%; mild, EF 46-50%; moderate, EF 41-45%;severe, EF≤ 40%. Cox regression models adjusted for prognostic indicators were fitted.
Results: As compared with patients without LVSD, the 46% with LVSD had higher rates of M and SD (12.3% vs 5.8%% and 3.4% vs 1.3%). There was a graded association between LVSD, M and SD. Treatment with n-3 reduced M as well as SD in patients with and without LVSD (heterogenity test NS). When we assessed the effect of n-3 on SD according to the grade of LVSD, the test for trend was statistically significant thus indicating a concentrated effect of n-3 in patients with progressively worsening of LV systolic function.
Conclusions: mild/moderate LVSD is a common feature of post-MI patients and is associated with increased risk of M and SD. Treatment with n-3 decreased M and SD in patients with and without LVSD. Progressively increasing LVSD is associated with elevated risk of SD and with increased benefit from n-3



1088-121 Improved Myocardial High-Energy Phosphate Metabolism Induces by Partial Free Fatty Acid Inhibition in Patients With Heart Failure

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Background. The addition of the partial free-fatty acid inhibitor trimetazidine to standard treatment, has beenshown to effectively improve left ventricular function in patients (pts) with heart failure. The beneficial effect of trimetazidine has been attributed to preservation of cardiac phosphocreatine (PCr) and adenosine triphosphate (ATP) intracellular levels. Aim of this study was to assess the effects of trimetazidine on PCr and ATP concentrations in pts with heart failure.
Methods. Twelve pts (1 female) with heart failure (6 post-ischemic, 5 hypertensive, 1 dilated cardiomyopathy) on conventional therapy were randomised in a double blind, cross-over study to placebo or trimetazidine (20mg t.i.d) for 2 periods of 90 days At the end of each period, all pts underwent exercise testing, 2D-echocardiography and cine magnetic resonance imaging and spectroscopy (MRS). NYHA class, ejection fraction (EF), maximal rate-pressure product (RPP) and METS were evaluated. Concentrations of PCr and ATP were determined by ^{31}P-MRS with spatial localization with optimum pointspread function.
Results. On trimetazidine, NYHA class decreased from 3.1±0.2 to 2.5±0.5 (p=0.009) while exercise time (from 323±148 to 334±156 sec, p=0.36), peak RPP (from 17462±3601 to 18894±4893 mmHgxbpm, p=0.09), METS (from 7.44±1.84 to 8.78±2.72, p=0.034) and EF (34±10 vs 39±10%, p=0.037) increased. The mean cardiac PCr/ATP ratio was 1.36±0.35 with placebo but was increased by 19% to 1.62±0.45 (P=0.04) with trimetazidine.
Conclusions. In conclusion, trimetazidine improves left ventricular function and symptoms in pts with heart failure. These beneficial effects are likely related to the observed trimetazidine-induced improvement of cardiac high-energy phosphate metabolism. Metabolic modulation with partial fatty acid inhibitors can represent a new therapeutic complement in heart failure and should be tested in large scale trials.

1088-122 Augmentation of Glucose Metabolism With Perhexiline Improves Maximal Oxygen Consumption and Quality of Life in Patients With Nonischaemic Dilated Cardiomyopathy

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Background
Despite considerable advances in pharmacotherapy, chronic heart failure (CHF) remains a major cause of morbidity and mortality. Additional effective therapies are needed. Glucose metabolism is more oxygen efficient than Free Fatty Acids (FFA) metabolism at generating ATP. CHF leads to a shift in metabolic substrate use from FFA to glucose but whether this represents an adaptive or maladaptive process is unclear. The anti-anginal drug perhexiline further augments glucose metabolism by inhibiting mitochondrial FFA uptake. We hypothesize that augmentation of glucose metabolism is beneficial in CHF and associated with an improvement in symptoms, and peak exercise oxygen consumption (VO_2 max), an important measure of both prognosis and functional status.
Methods
This was a randomised double blind placebo controlled trial. 24 patients with Dilated Cardiomyopathy, angiographically normal coronary arteries, and optimally medicated CHF (NYHA II-III, EF<40%) were randomised to perhexiline (n=12) or placebo (n=12) for 2 months. Cardiopulmonary exercise testing with respiratory gas analysis and completion of the Minnesota Living with Heart Failure Questionnaire (MLHFQ) were performed before and after treatment.
Results
Expressed as mean ± SEM. VO2max was similar at baseline in the perhexiline and placebo groups (17.1 ± 1.1 vs. 16.0 ± 1.3 mls/kg/min). Following treatment, VO2max was unchanged in the placebo group (16.1 ± 1.5 mls/kg/min) but increased in the perhexiline group (19.6 ± 1.5 mls/kg/min). ANCOVA using baseline values as covariates demonstrated a significant effect of perhexiline vs. placebo on VO2max; p=0.03. MLHFQ scores were similar at baseline in the perhexiline and placebo groups (45.4 ± 7.9 vs. 47.2 ± 6.5 respectively) and fell markedly following treatment in the perhexiline group (30.7 ± 6.9) but not in the placebo group (42.8 ± 6.5); ANCOVA, p=0.03.
Conclusion
Treatment with perhexiline leads to an improvement in VO2max and quality of life in Dilated Cardiomyopathy. This benefit suggests that augmentation of glucose metabolism could be beneficial in heart failure even in the absence of underlying ischaemia and represents a potential future treatment strategy.

1088-123 Cancion Cardiac Recovery System: Hemodynamic and Renal Effects

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Background: The purpose of this study was to examine the hemodynamic effects of the Cancion Cardiac Recovery System (CRS), a novel extracorporeal device that superimposes continuous aortic flow on existing pulsatile flow. We hypothesized that by reducing LV afterload and increasing aortic flow the CRS would improve the hemodynamics in patients with acutely decompensated chronic heart failure who were refractory to standard medical therapy. **Methods:** The inflow to the CRS centrifugal pump was via a percutaneous femoral arterial cannula and outflow was via either a graft cannula anastomosed to the left axillary artery (n=4) or percutaneously through the femoral artery (n=3) via an aortic pigtail cannula. **Results:** Seven patients were placed on the CRS and supported for an average of 66 hours (24 hrs to 5 days) with pump flows between 1.2 and 1.5 (mean, 1.3) l/min. Hemodynamic data are shown in the Figure. Data during and after CRS suggest that the PCWP vs CI relationship is reset.**Conclusions:** The Cancion CRS, a novel form of cardiac assistance, acting through a low-flow, continuous aortic flow loop, markedly improved PCWP, CI and renal function in patients with refractory heart failure. Hemodynamic and renal functional improvement persisted following discontinuation of the CRS. These results suggest that the CRS may be an effective treatment for decompensated chronic heart failure.